REMARKS

Claims 47-58 are pending in this application. Claims 59-74 have been cancelled from the application without prejudice in response to the Examiner's Restriction Requirement. Claim 47 has been amended to provide antecedent basis for the term "liquefied embedding medium". Claims 51 and 57 have been amended to overcome the Examiner's rejection of those claims under Section 112, second paragraph. These amendments do not narrow the scope of the application claims nor do they add new matter to the application.

The claims are presented above in the "Revised Amendment Format" recently adopted by the USPTO. For the Examiner's convenience, a clean set of all pending application claims is attached as Appendix A to this Reply.

By way of review, the Applicants have discovered a new method and apparatus for removing embedding media from biological samples on automated instruments prior to further manipulations of the biological sample.

The Examiner's claim objections and rejections are traversed or overcome as set forth below.

I. THE RESTRICTION REQUIREMENT

The Examiner required a restriction of the claims to one of two inventions. The Applicants have elected to proceed with the examination of claims 47-58, drawn to a method of removing embedding medium from a biological sample. The non-elected claims 59-74 have been cancelled from this application without prejudice.

II. THE SECTION 112, 2nd PARAGRAPH REJECTION OF CLAIMS 51 & 57

The Examiner rejected claims 51 and 57 under 35 U.S.C. Section 112, second paragraph as being indefinite. Specifically, the Examiner objected to the use of the trade names Triton X-100, Tween and Brij in the claims.

The Examiner's claim objection has been overcome, in part, by canceling the terms

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"Triton X-100" "Brij', and "Tween" from claims 51 and 57 and replacing the cancelled term with the chemical names of the surfactants represented by the tradenames. The specification has similarly been amended a page 16, lines 22-23. A listing of surfactant tradenames and their corresponding chemical names is included as Exhibit A to this Reply. Replacing the tradenames with the surfactant chemical names in the specification and claims does not add new matter to the application.

III. TRAVERSE OF THE ANTICIPATION REJECTION

The Examiner rejected pending application claims 47-58 under 35 U.S.C. 102(b) as being anticipated by Zhang et al. (WO 95/24498). The Examiner also rejected claims 47-50, 52-56, and 58 for being anticipated by Key et al. (U.S. Patent No. 5,244,787) or for being anticipated by the Stross et al. article. The Applicants respectfully traverse the Examiner's anticipation rejections.

A. The Claims Are Not Anticipated By Zhang et al.

Zang et al. does not anticipate any of the pending application claims. The Zang et al. reference discloses a process for removing an embedding media from a biological sample with a solvent at low temperatures. In contrast, the claimed invention is directed to a method that liquefies the embedding media in order to remove it from a biological sample.

The Zang et al. reference is directed to:

> new dewaxing solvent compositions for removal of paraffin or other waxes from wax-embedded biological specimens for histochemical or other analyses.

(Page 3, lines 5-7). The dewaxing solvents used contain a "paraffin-solubilizing organic solvent". The paraffin solubilizing organic solvent must be a solvent that is:

> . . . capable of dissolving paraffin used for embedding biological samples.

(Page 4, lines 28-29). According to Zang et al., the process:

> is typically and conveniently carried out a room temperature, without the need for a temperature controlled bath, a more precise control of the required time for satisfactorily dewaxing and washing is available if the temperature-controlled baths are used. Heating decreases processing time. Operable temperatures range from 5°

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to 50°, preferably from about 15° to about 45°, and more preferably from about 25° to 40°C.

(Page 11, lines 19-24). Zang et al. clearly discloses deparaffinization methods that use organic solvents to **dissolve** paraffin at low temperatures.

In contrast, the claimed invention is directed to a deparaffinization method in which a biological sample is heated to a temperature at or above the embedding medium's melting point to liquefy the embedding medium. (See, e.g., claim 47). A non-organic liquid is then applied to the sample to flush the liquefied embedding medium from the biological sample. (Page 13, lines 13-29). In order to liquefy the embedding medium the biological sample will generally need to be heated to a temperature in excess of 50°C. (Page 12, lines 6-11).

The claimed methods include the step of heating a paraffin-containing biological sample to a temperature in excess of the melting point of the embedding medium temperature in order to liquefy the embedding media. Zang et al. does not disclose this claimed step. For at least this reason, Zang et al. cannot anticipate any application claim.

B. Key et al. Does Not Anticipate Any Application Claims

Key et al. does not disclose or suggest the claimed deparaffinization process. Moreover, Key et al. is not directed to a biological sample deparaffinization process. Instead, Key et al. is directed to an antigen retrieval method that is performed following sample deparaffinization. Indeed, Key et al. mentions sample deparaffinization only in passing when it notes:

> Typically paraffin is removed from the paraffin-embedded tissue, for example by melting of the paraffin (which has a melting point of approximately 55-60 degrees C depending upon the type of paraffin) or dissolving the paraffin in an appropriate solvent, such as chloroform or xylene.

(Key et al., Col. 5, lines 54-59). This is the only excerpt from the Key et al. reference that discusses deparaffinization. The remaining portions of the Key et al. reference cited by the Examiner in rejecting claims over Key et al. (Col. 5, line 60 to Col. 6, line 43) has nothing to do with deparaffinization. Instead, the portions cited are a discussion of antigen recovery methods. Thus, Key et al. discloses nothing more than melting paraffin in a biological sample. Key et al.

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does not disclose deparaffinization of any kind in the presence of a non-organic liquid as claimed. Therefore, Key et al. cannot anticipate any pending application claim.

the deparaffination is in presence of a non-organic liquid not

C. The Claims Are Not Anticipated By The Stross et al. Article

The Stross et al. article is unrelated to the claimed invention because it does not discuss deparaffinization. The Stross et al. article excerpt cited by the Examiner – at page 107, first paragraph states:

> A Histokinette type E7326 (British American Optical Corporation), which had previously been used for a number of years in the histology department for tissue processing and impregnation with paraffin wax, was used (fig 1). This machine has 12 "stations" for siting baths of reagents around the circumference of a circular platen and is equipped with heating elements to melt the paraffin wax contained in the later baths.

The excerpt cited has nothing to do with removing paraffin from biological samples. The excerpt merely describes a machine that was modified by the authors for a new use that has nothing to do with deparaffinization. Indeed, in the methods discussed in Stross et al., the heaters have been removed in the modified system, so the tanks cannot be heated. Furthermore, the article excerpt unequivocally states that the original apparatus was used to impregnate tissues with paraffin. Thus, the Stross et al. article does not anticipate any application claim because the article is not directed to a deparaffinization process so the article fails to disclose any steps of the claimed invention.

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CONCLUSION

In view of the amendments and statements in favor of claim patentability presented above, it is believed that all pending claims 47-58 of this application are allowable and that all claim rejections and objections should be withdrawn. Favorable reconsideration and allowance of all application claims is, therefore, courteously solicited.

Respectfully submitted,

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Dated: February 7, 2003

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Appendix A

Complete Set Of Pending Application Claims

Claims 47-58 are pending in this application

47. A method of removing embedding medium from a biological sample, the method comprising the steps of:

heating the biological sample containing embedding medium to a temperature at or above the embedding medium's melting point to form a liquefied embedding medium; and

applying a non-organic liquid to the biological sample to separate the liquefied embedding medium from the biological sample, wherein said non-organic liquid has a density greater than that of the liquefied embedding medium.

48. The method of claim 47, wherein the non-organic liquid comprises water.

49. The method of claim 47, wherein the non-organic liquid comprises a detergent.

50. The method of claim 49, wherein the detergent comprises ionic or non-ionic surfactants.

51. The method of claim 50, wherein the ionic or non-ionic surfactants are selected from the group consisting of octylphenoxypolyethoxy (5) ethanol, polyoxyethelene(20)sorbitan, polyoxyethelene(23) dodecyl ether, sodium dodecylsulfate and saponin.

52. The method of claim 47 wherein the embedding medium comprises paraffin wax.

53. A method of removing embedding medium from a biological sample, the method comprising the steps of:

applying a non-organic liquid to a biological sample; and

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heating the biological sample containing embedding medium to a temperature at or above the embedding medium's melting point.

54. The method of claim 53, wherein the non-organic liquid comprises water.

55. The method of claim 53, wherein the non-organic liquid comprises a detergent.

56. The method of claim 55, wherein the detergent comprises ionic or non-ionic surfactants.

57. The method of claim 56, wherein the ionic or non-ionic surfactants are selected from the group consisting of octylphenoxypolyethoxy (5) ethanol, polyoxyethelene(20)sorbitan, polyoxyethelene(23) dodecyl ether, sodium dodecylsulfate and saponin.

58. The method of claim 53, wherein the embedding medium is paraffin wax.

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